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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/800,448 | 03/05/2001 | Santu Bandyopadhyay | A34065 | 2808 |
| 21003 | 7590 | 03/24/2006 | | |
| BAKER & BOTTS 30 ROCKEFELLER PLAZA NEW YORK, NY 10112 | | | | |
| | | | EXAMINER EWOLDT, GERALD R | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1644 | |

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/800,448

Applicant(s)

BANDYOPADHYAY ET AL.

Examiner

G. R. Ewoldt, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14-21,23-26,28-36 and 38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14-21,23-26,28-36 and 38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 10/11/05 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment and remarks filed 10/11/05 have been entered.
2. Claims 14-21, 23-26, 28-36, and 38 are pending.
3. In view of Applicant's amendments, the previous rejections under the first and second paragraphs of 35 U.S.C. 112 have been withdrawn. Additionally, in further in view of Applicant's amendments, the previous rejections under 35 U.S.C. 102(b) and 103(a) have been withdrawn. In particular, the addition of a new step requiring monitoring and confirming mature dendritic Langerhans cells (DLCs) has rendered the claimed method novel and non-obviousness in view of the prior art.
4. The following are new grounds of rejection.
5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 14-21, 23-26, 28-36, and 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the claimed method would result in mature DLCs as claimed.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must

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be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

A review of the specification discloses that the method of the instant claims comprises culturing monocytes or bone marrow cells with platelets, said culture resulting in mature DLCs. A review of the art shows that bone marrow includes multiple cell types including stromal cells, red blood cells, and white blood cells, including monocytes, but also including eosinophils and other unrelated white blood cells, see for example, *Wikipedia*. It is unclear how unrelated and terminally differentiated cell types such as red cells or stromal cells can be cultured into mature DLCs. Given that the specification discloses only the use of human monocytes and undefined mouse bone marrow cells, and further given that there is no evidence of record that cells can be dedifferentiated and transformed into an unrelated cell type, it is most likely that only the monocytes found in the mouse bone marrow actually cultured into mature DLCs. Accordingly, the method of the instant claims are not enabled as broadly claimed.

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Additionally, there is no evidence of record that the method of the instant claims actually results in a mature DLC. As set forth in Brand et al., LC-specific markers, e.g., the Lag antigen were known in the art at the time of the invention. Curiously, the product cells of the instant claims were not assayed for such markers to confirm their identity. Several markers were, however, assayed. As further set forth in Brand et al., CD1a should be found on essentially all DLCs, yet the specification discloses that "only approximately 20%" of the product cells of the instant claims displayed this marker. The reference further teaches that a mature DLC would also be expected to express CD80, yet again, the specification discloses that "only approximately 20%" of the product cells of the instant claims displayed this marker. Likewise, a mature DC of any type would be expected to express high levels of CD83, yet again, the specification discloses that "only approximately 20%" of the product cells of the instant claims displayed this marker. Accordingly, in view of the disclosed results, it is unclear how the cells obtained by the method of the instant claims can be considered to be DLCs.

Of further note is the cell type to which the asserted DLCs of the claimed method are compared, i.e., monocytes matured in GM-CSF and IL-4. As set forth in Romani et al., the culture development of LCs from precursor cells in culture requires either TNF α , or more preferably, TGF β 1. Absent either of these cytokines it is unclear what the cells of the claimed method were actually compared to. It is clear, however, that they were not compared to LCs.

Given the demonstrated unpredictability of the art, i.e., that differences in the cytokine milieu in which precursor DCs are cultured results in different cell products, claims reciting a method of culturing cells resulting a single, specific cell type such as this, absent any sort of showing, or even sound scientific reasoning, in support, must be considered unpredictable and requiring of undue experimentation.

7. Claims 14-21, 23-26, 28-36, and 38 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed

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invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) a method comprising ... monitoring the cultured cells for the appearance of dendritic morphology and confirming the presence of dendritic processes, wherein the presence of dendritic morphology and processes indicates growth of mature dendritic Langerhans cells, (Claims 14, 23, 28-30 and 32).

B) a method ... absent a step comprising incubating at about 30° to about 40°, (Claims 23, 29, 30, and 32).

C) a method ... wherein the peripheral blood monocytes and/or bone marrow cells and the platelets may be independently selected from the group of rat cells and mouse cells, (Claim 30).

D) a method ... wherein more than about 50% display reactivity to anti-HLA-DR, anti-CD40, and anti-CD86 monoclonal antibodies and approximately 20% of the mature dendritic cells display reactivity to anti-CD1a, anti-CD80, and anti-CD83 monoclonal antibodies (Claim 32).

Regarding A), Applicant indicates support for the limitation at pages 7-9 of the specification.

Pages 7-9 of the specification discloses only a single experiment employing only human monocytes incubated with autologous platelets in serum free medium. The cite does not disclose the broad method of the instant claims. Further, the cite does not disclose a specific "monitoring" of the appearance of dendritic morphology nor the specific "confirming" the presence of dendritic processes, nor that this "monitoring" and "confirming" would be used as an indication of the growth of mature dendritic Langerhans cells.

Regarding B), in all disclosures regarding methods of producing mature DLCs, said method includes incubating at about 30° to about 40°, see for example, page 3.

Regarding C), the specification discloses only a method of producing mouse DLCs employing rat platelets and not the specific combinations of the claims, e.g., producing rat DLCs employing rat bone marrow cells and mouse platelets.


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Regarding D), the cite at page 8 relied on for support, discloses only a single experiment employing only human monocytes incubated in serum free medium with autologous platelets. Additionally, the cite discloses "only approximately 20%" and not the "approximately 20%" of the claim. This is not the broad method of the claim.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

10. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Inquiries of a general nature may also be directed to the Technology Center 1600 Receptionist at (571) 272-1600.



G.R. Ewoldt, Ph.D.
Primary Examiner
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